DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[Docket No. CDC-2022-0003]

Policy Statement for Biosafety Level 4/Animal Biosafety Level 4 Laboratory Verification; Notice of Availability

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Notice.

SUMMARY: The Centers for Disease Control and Prevention (CDC), in the Department of Health and Human Services (HHS), announces the availability and implementation of the final Biosafety Level 4 (BSL-4)/Animal BSL-4 (ABSL-4) verification policy. The policy statement assists individuals and entities in verifying that the facility design parameters and operational procedures, including heating, ventilation, and air conditioning (HVAC) systems, in BSL-4 and/or ABSL-4 laboratories are functioning as intended to meet the biosafety sufficiency requirement in the HHS/CDC select agent and toxin regulations.

DATES: The compliance date for this Policy is [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Samuel S. Edwin Ph.D., Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop H21-4, Atlanta, Georgia 30329. Telephone: (404) 718-2000. Email: lrsat@cdc.gov.

SUPPLEMENTARY INFORMATION: On January 19, 2022, CDC published a notice in the *Federal Register* (87 FR 2791) requesting public comment on a draft policy statement on BSL-4/ABSL-4 laboratory verifications standards, including HVAC, to aid individuals and entities in verifying that these laboratories are properly functioning. HHS/CDC received comment on the draft policy statement concerning BSL-4/ABSL-4 verification requirements from seven commenters. The commenters were from academia, industry, city/local government, and the public.

Summary of Public Comments

In general, commenters supported the draft policy but had specific suggestions on wording and revisions. Please see a summary of the comments and our responses below.

Comment: One commenter suggested changing the subject to include BSL-3 Agriculture.

Response: HHS/CDC notes that an established BSL-3/ABSL-3 Verification Policy already exists (https://www.cdc.gov/cpr/ipp/docs/Policy_Import_BSL3_ABSL3_Verification.pdf). Thus, HHS/CDC made no changes based on this comment.

Comment: One commenter recommended that Heating, Ventilation, and Air Conditioning (HVAC) be referred to as "Building and Mechanical, Electrical, and Plumbing (MEP) systems."

Response: HHS/CDC disagreed with this recommendation because the term "HVAC" is more universally referenced. No changes were made to the policy due to this comment.

Comment: HHS/CDC received comment regarding clarification and testing of the HVAC system only after major changes or every ten years.

Response: HHS/CDC agreed with the commenter to provide the clarification and has updated the policy to state that entities must ensure HVAC verification is performed and documented "after major changes to ensure operational parameters are maintained." The policy includes examples of major changes that can be referenced. HHS/CDC disagreed with the other comments regarding increasing the testing requirement to every ten years.

Comment: A commenter discussed primary and secondary fans versus parallel HVAC fans and how setup depends on different facility configurations.

Response: HHS/CDC agreed with the comment about configuration of HVAC fans and included "or failure of parallel fans depending on facility configuration" in the policy.

Comment: Commenters requested that examples be provided for major changes and that HHS/CDC provide a list of repairs to HVAC control system components that require verification testing.

Response: HHS/CDC agreed with providing examples and has updated the policy to include examples of major changes that can be referenced. Modifications include repairs or replacing a component to the HVAC to ensure that the system is fully

operational. HHS/CDC also revised the policy to state "systems" instead of "components." Entities should ensure all HVAC systems are operational, and because systems vary, the components of the system also vary from entity to entity; therefore, HHS/CDC will not be providing a universal list of repair of HVAC control system components.

Comment: Another commenter suggested using a risk assessment-based approach to determine if failure testing is required after resolving a major problem.

Response: HHS/CDC disagreed with the comment regarding a risk assessment-based approach to determine if failure testing is required after a major problem. As such, HHS/CDC made no updates to the policy. HHS/CDC understands the commenters' concerns regarding a disruption due to a major problem and then the need for the entity to perform HVAC operational verification. However, HHS/CDC believes it is essential to verify the system annually and after any significant modification to ensure operational parameters are maintained during both normal operating conditions and failure conditions to prevent air-flow reversals into non-containment areas (e.g., outside the containment boundary, hallways).

Comment: A commenter requested that HHS/CDC require an HVAC design verification process for "primary containment (suit and cabinet room's primary barrier equipment)" instead of secondary containment.

Response: HVAC is part of the facility safeguards, which is a secondary barrier; therefore, HHS/CDC will not be referring to this as primary containment. Secondary containment is defined by the 6th edition of the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) as the design and construction of the laboratory facility that provides a means of secondary containment of hazardous biological agents and toxins to protect personnel, the surrounding community, and the environment from possible exposure to hazardous biological agents and toxins.

Comment: A commenter recommended excluding small repairs, like-for-like replacement of smaller components, and minor automation system logic programming changes.

Response: HHS/CDC made no changes to the policy and agreed with the commenter that minor changes and small repairs mentioned above would not be considered major repairs.

Comment: Commenters suggested specific references be added to the list of systems to be tested/verified annually such as chemical shower, alarms, power source, communications, access systems, Air Pressure Resistant(APR) door gaskets, positive-pressure suits, water supply, and manual overrides tested (e.g., between mechanical and electronic door interlocks).

Response: HHS/CDC agreed with the commenters and updated the policy to reference these items.

Comment: Commenters requested the term “uninterrupted power supply" be changed to adequately reflect the meaning.

Response: HHS/CDC agreed with the commenters and changed the term to "automatically activated backup."

Comment: A commenter asked if room air pressure trend lines captured from the Building Automation System (BAS) could be used to demonstrate the absence of air reversal.

Response: HHS/CDC agreed and revised the policy to state that entities may use BAS records to demonstrate no airflow reversal from the BSL-4/ABSL-4 laboratory during transition from normal power to the automatically activated backup, emergency power supply.

Comment: Another commenter suggested the inclusion of emergency power stand-by systems (emergency generator and automatic transfer switch), uninterruptible power supply, and critical equipment with internal batteries (e.g., programmable logic control devices) to the minimum verification requirement for back-up power systems for HVAC.

Response: HHS/CDC agreed with the comment and revised the policy to include "routine maintenance programs and backup, power systems" to succinctly summarize the minimum verification requirements.

Comment: Commenters requested term "power failure" be changed to adequately reflect the meaning.

Response: HHS/CDC agreed with commenters and changed the term to "emergency power status."

Comment: A commenter stated that "only modifications in the programming sequence that affect how the laboratory reacts in

failure conditions should be required to be re-tested." The commenter further suggested that changes or updates such as "tuning PID loops, updates on coefficients that are imbedded in the sequence of operation, or the optimization of the logic to reduce the traffic of data in the system, should not require re-verification."

Response: HHS/CDC made no changes based on this comment. HHS/CDC is primarily interested in ensuring that all systems are working as designed after any major changes, which is a normal practice to ensure the system is fully operational.

Comment: A commenter suggested that the addition or removal of hard-ducted equipment (e.g., biological safety cabinets [BSCs], Class III BSC, or decontamination systems) without affecting the airflow balance of the room does not affect the operations, therefore no re-verification should be required.

Response: HHS/CDC made no changes based on the comment. Additions or removals should be tested to ensure repairs were effective even if one component was replaced.

Comment: A commenter stated that the methods for verification of primary containment integrity is unclear and needs to be clarified (specifically for primary containment of centrifuges and animal caging systems). The commenter further requested that the policy state what documentation or testing is needed for the verification.

Response: HHS/CDC made no changes to the policy based on the comment since there are no specific tests to determine

integrity. Centrifuges need to have safety cups and no leaks in the washers to ensure integrity of primary containment inside the centrifuge (BMBL 6th edition, Inadvertent Toxin Aerosols). Animal cages need to be designed to allow recirculation of air into the room after high-efficiency particulate air (HEPA) filtration (BMBL 6th edition, Part 3: Biological Safety Cabinets). While there are no specific tests to determine integrity, HHS/CDC recommends that the entity verifies the animal caging systems and centrifuge, and its components, are working as designed.

Comment: Commenters requested to clarify the meaning of BSCs with an HVAC connection "not working properly." A commenter asserted that the observation or evidence that the BSC is not working properly is more of an issue with the certification and maintenance of the equipment and not the HVAC system, therefore, it is not a major problem and does not require re-verification.

Response: HHS/CDC agreed with the commenters to clarify the meaning of "not working properly" and revised the policy to read "observation or evidence that BSCs with an HVAC connection (hard duct or thimble) are not working as designed." HHS/CDC disagreed with the commenter regarding reverification. When major repairs are made to the BSC including replacing components of the BSC, the entity should test the system to ensure repair was effective and does not compromise the functionality of the HVAC system.

Comment: Commenters requested clarification on verifying BAS-programmed alarm communication as part of the BSL-4/ABSL-4

facility verification. One commenter recommended that verification of BAS programmed alarms should be tested only initially.

Response: HHS/CDC did not make any changes based on the comments. Verification of the BAS-programmed alarm communication should include assurance that if an alarm occurs, the strobes, lights, or audibles are activated. Testing annually ensures all parameters that are important to maintain containment have a functioning alarm.

Comment: A commenter provided editorial changes for clarity to paragraph A, Effluent, tissue, autoclave, and decontamination systems, under section 3 (confirmation that decontamination systems are operating as designed [e.g., autoclave, room decontamination systems, tissue digesters, liquid effluent systems, and chemical showers]). Specifically, the commenter recommended:

- 3. A. i: Change to Annual verification that system operational parameters have not changed from biologically validated conditions (e.g., volume, pressure, temperature settings)
- 3. A. iii: Change to Annual certification testing of associated HEPA filters, if applicable (e.g., operating vent, pressure relief vent, chamber effluent/vent)
- 3. A. iv: Change to Annual verification that system failure, emergency communication systems are operating as designed (e.g., alarms, leak detection)

- 3. A. v: Change to Verify appropriate filter media is selected and maintained annually (e.g., HEPA, polytetrafluoroethylene [PTFE])

Another commenter agreed that 3. A. v. should be rewritten for clarity and stated that the sentence should refer to "HEPA, however, it should instead be revised in terms of efficiency and particle size since HEPA filters are at least 99.97% of airport particles 0.3 micrometers, while PTFE filters have 99.99% efficiency of airborne particles 2.5micrometers in diameter."

- 3. A. vi: Another commenter stated that this was unclear and needs to be clarified to state specifically what document/test needs to be provided to meet this requirement.

Response: HHS/CDC agreed with the editorial changes, updated the policy based on these changes, and clarified 3. A. v. to read "v. Verify appropriate filter media is selected and maintained annually (e.g., HEPA, PTFE)." However, HHS/CDC disagreed with suggestion to revise 3. A. iv. "annual verification that system failure alarms are operating as designed" because the language is clear as written and communication is more encompassing than alarms. HHS/CDC agreed with the commenter to clarify 3. A. vi. to read, "Implementation of risk-based preventative maintenance for other equipment that is critical to containment components, but is not specifically included above (e.g., cook tanks, etc.)."

Comment: A commenter requested to clarify decontamination systems by adding decontamination rooms and chambers.

Response: HHS/CDC made no changes to the policy based on the comment because some facilities may not have these rooms or chambers.

Comment: A commenter responded that room decontamination should be validated upon each use and not rely on annual verifications as a substitution, since parameters can shift slightly from use to use (i.e., atmospheric moisture or room temperature).

Response: HHS/CDC agreed with commenter; however, no changes were made based on this comment since the policy notes that this is an annual verification of the room decontamination system and biological indicators are already mentioned for this reason.

Comment: Commenters suggested wording changes for annual verification requirement for certification of laboratory HVAC, plumbing vent line, and decontamination system filters, stating that there are no written standards by which to certify BSL-4/ABSL-4 laboratories.

Response: HHS/CDC agreed with the commenters and made the change to the policy.

Comment: A commenter requested that "established" specifications be changed to "approved design" specifications.

Response: HHS/CDC agreed with the commenter and revised the policy.

Comment: Commenters requested adding the verification requirement for "pressure decay testing."

Response: HHS/CDC agreed with the commenters and included that pressure decay testing may be used to identify and confirm proper operation of various BSL-4/ABSL-4 containment boundary points of failure (e.g., penetrations, cracks, breaks, APR doors, HEPA isolation dampers, etc.).

Where can this document be found?

This policy document is available at the Federal Select Agent Program website at www.selectagents.gov.

Legal Authority

HHS/CDC is issuing this policy under the authority of sections 201-204 and 221 of Title II of Public Law 107-188, (42 U.S.C. 262a).

Tiffany Brown,

Acting Executive Secretary,

Centers for Disease Control and Prevention.

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